

Appl. No. 09/700,712
Amendment dated: January 24, 2005
Reply to OA of: September 23, 2004

Amendments to the Specification:

On page 4, please replace the paragraphs under the heading "Short description of the drawings" with the following amended paragraphs.

~~Figure 1 shows Figures 1a and 1b show~~ the nucleotide sequence SEQ ID NO:1 of the *thy A* gene of *Vibrio cholerae*.

Figure 2 shows the nucleotide sequence SEQ ID NO:2 of the 5'-flanking region of the structural *thy A* gene of *Vibrio cholerae*.

Figure 3 shows the nucleotide sequence SEQ ID NO:3 of the 3'-flanking region of the structural *thy A* gene of *Vibrio cholerae*.

Figure 4 shows the amino-acid sequence SEQ ID NO:4 of the protein encoded by the structural *thy A* gene of *Vibrio cholerae*.

Figure 5 shows the amino-acid sequence SEQ ID NO:5 of the protein encoded by the 5;-flanking region of the structural *thy A* gene of *Vibrio cholerae*.

Figure 6 shows the cloning of a *Eco*RI/*Hind*III fragment containing the *V.cholerae thyA* gene in pUC19.

Figure 7 shows a comparison of *thyA* gene products from *E. coli* [16], *V. cholerae* and *H. influenzae* [17] showing the high degree of homology between *V. cholerae* and *H. influenzae* compared with *E. coli*.

Figure 8 shows the insertion of a Kan^R-resistance gene block in the *Pst*I site of the *V.cholerae thyA* gene in pUC19.

Figure 9 shows PCR to generate a *thyA* -Kan fragment with *Xba*I ends.

Figure 10 shows ligation of the *thyA*-Kan fragment with *Xba*I ends in plasmid pNQ705.

Figure 11 shows partial deletion of the *thyA* gene and the start of the Kan gene in pNEB193.

Figure 12 shows *Xba*I cleavage to excise the Δ *thyA* Δ Kan gene from pNEB193, ligation into *Xba*I restricted pDM4.

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Figure 13 shows an outline of a strategy to completely delete the *thyA* gene of *V. cholerae*.

Figure 14 shows insertion of the 5' region upstream of *thyA* in pMT-SUICIDE 1; generation of pMT with 5 prim.

Figure 15 shows insertion of the 3' region downstream of *thyA* in pMT with 5 prim; generation of pMT Δ *thyA* *V.cholerae*.

Figure 16 shows the expression vector pMT-eltB(*thyA*) used for expression of LTB in *V. cholerae* JS1569 Δ *thyA*.

Figure 17 shows the expression vector pMT-GST(*thyA*) used for expression of GST in *V. cholerae* JS1569 Δ *thyA*.